#790 Separating the neural contributions to fMRI signal through Neural Prior Recovery.

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Background

- Standard confound correction consists of modeling and regressing confounds, but, it is unclear whether it can account for confounds while preserving neural activity (Power et al. (2020). Cereb Cortex).

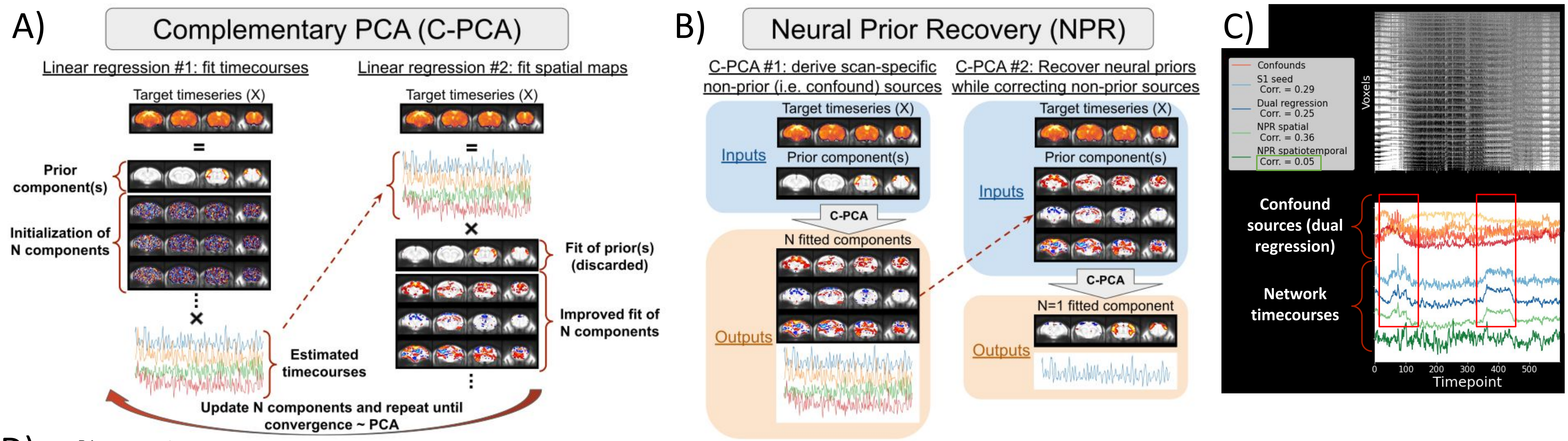
Alternative solution: isolate pre-defined neural sources (i.e. neural priors) from all other sources

- **Sub-goal 1, reliability:** Model scan-specific fMRI confounds in all forms (spatial and temporal)
- **Sub-goal 2, specificity:** maximize the relationship of recovered to neural activity
- **Sub-goal 3, generalizability:** automated framework with robust performance across datasets

Dataset and processing software

- **Multi-site dataset: representative survey of data quality issues**; 17 sites (5 not included); N=15 scans per site (Grandjean et al. (2020). NeuroImage.)
- **Simultaneous mesoscale calcium imaging and fMRI:** 10 subjects, 3 session X 9 runs per subject; with excitatory cell calcium marker (SLC)
- **Processing:** RABIES (https://github.com/CoBrALab/RABIES)

Algorithm Development



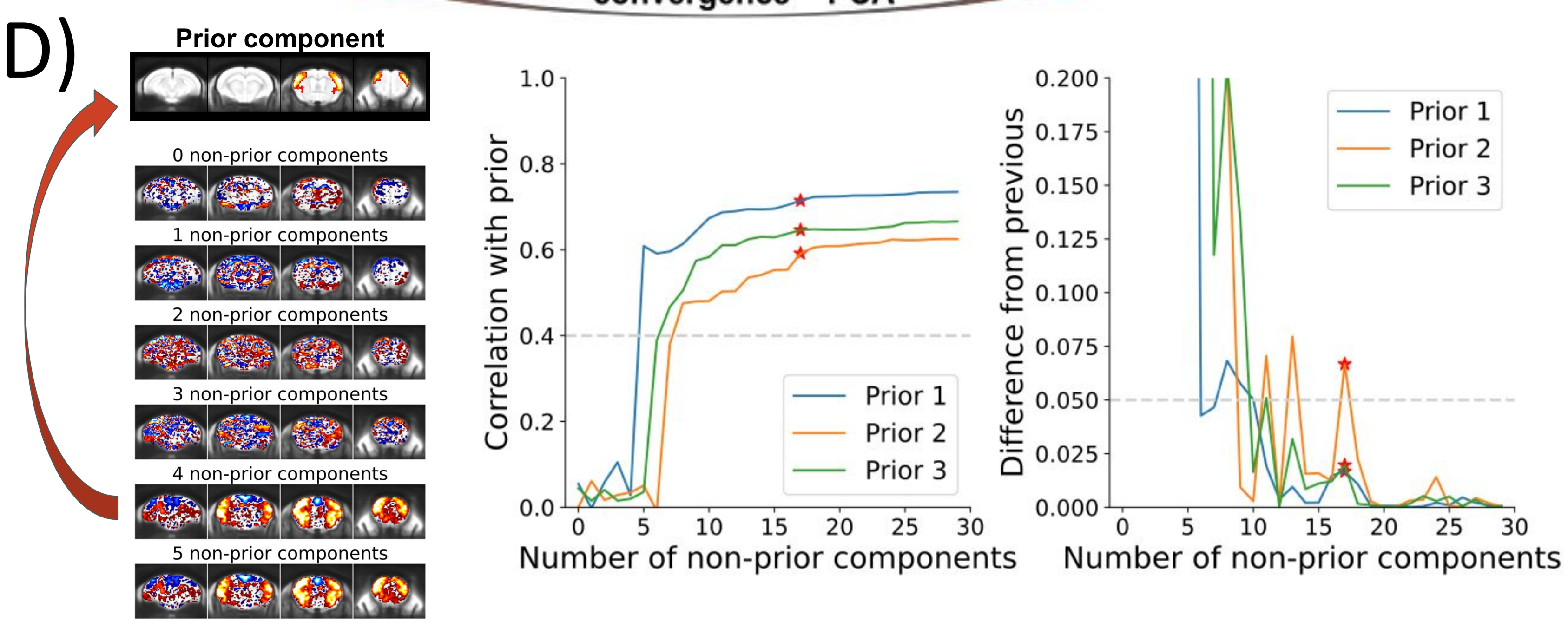


Figure 1: A) Complementary principal component analysis (C-PCA). Dual regression (regress spatial components, then regress the obtained component timecourses (Nickerson et al. (2017). Front Neuroscience)) can be iterated to approximate PCA, i.e. a set of components which maximize variance explained (Hardt (2014). IEEE 55th Annual Symposium). With this framework, we can introduce pre-defined prior components at each iteration, hence accounting for the priors and driving the convergence of other components towards a separate set differing from the priors. **B)** The Neural Prior Recovery (NPR) algorithm. C-PCA is used in two steps: 1) neural priors of interest are provided as input, and C-PCA finds all non-prior sources (i.e. confounds), 2) the non-prior sources are then provided as priors, so that the neural source can be recovered. **C)** To account for both spatially and temporally-defined confound signatures (Ciric et al. (2018). Nature Protocol) in the first NPR step, C-PCA is conducted twice for computing temporal and then spatial components (i.e. spatiotemporal NPR). **D)** On the left, example of convergence for NPR after accounting for 4 non-prior components. On the right, convergence criteria exemplified in the same scan for 3 priors simultaneously (**criterion 1:** spatial correlation between output and the neural prior; **criterion 2:** the difference between the previous and current output (i.e. 1 - their correlation)).

Result 1: automatize confound correction

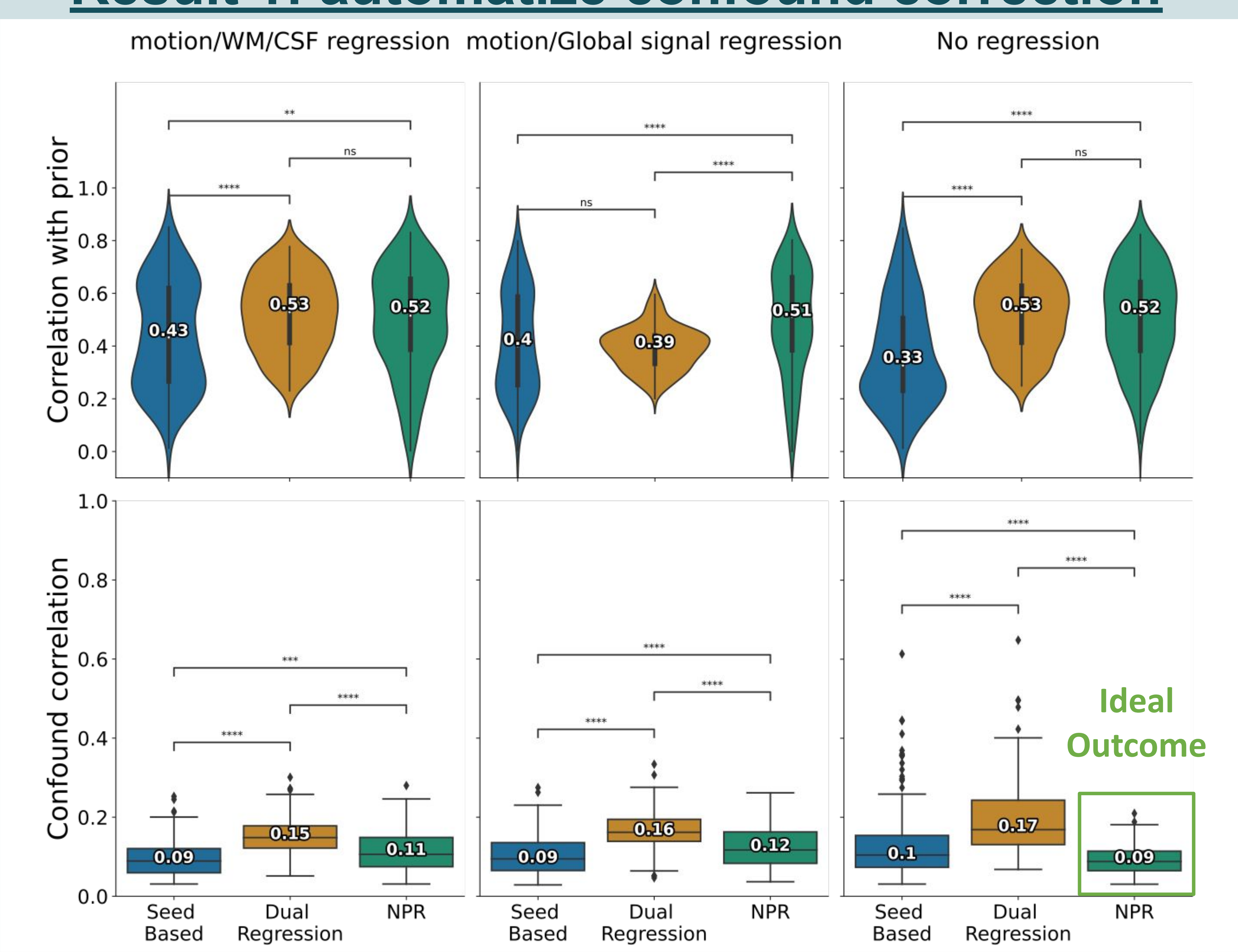


Figure 2: Impact of confounds on connectivity analyses, tested across 12 mouse fMRI acquisition sites. The top plot displays the distribution of correlations between the scan-level fits and prior network maps. The bottom plot shows the mean temporal correlation between the network timecourse and a set of confound component timecourses measured through dual regression (using group-ICA confound components described in Desrosiers-Gregoire et al. (2022. bioRxiv.); see example in **figure 1C**). Nuisance regression was varied (3 different columns) to include the regression of 6 motion parameters + WM/CSF signal, 6 motion parameters + global signal, or no regression.

Result 2: maximize relationship to calcium tracer

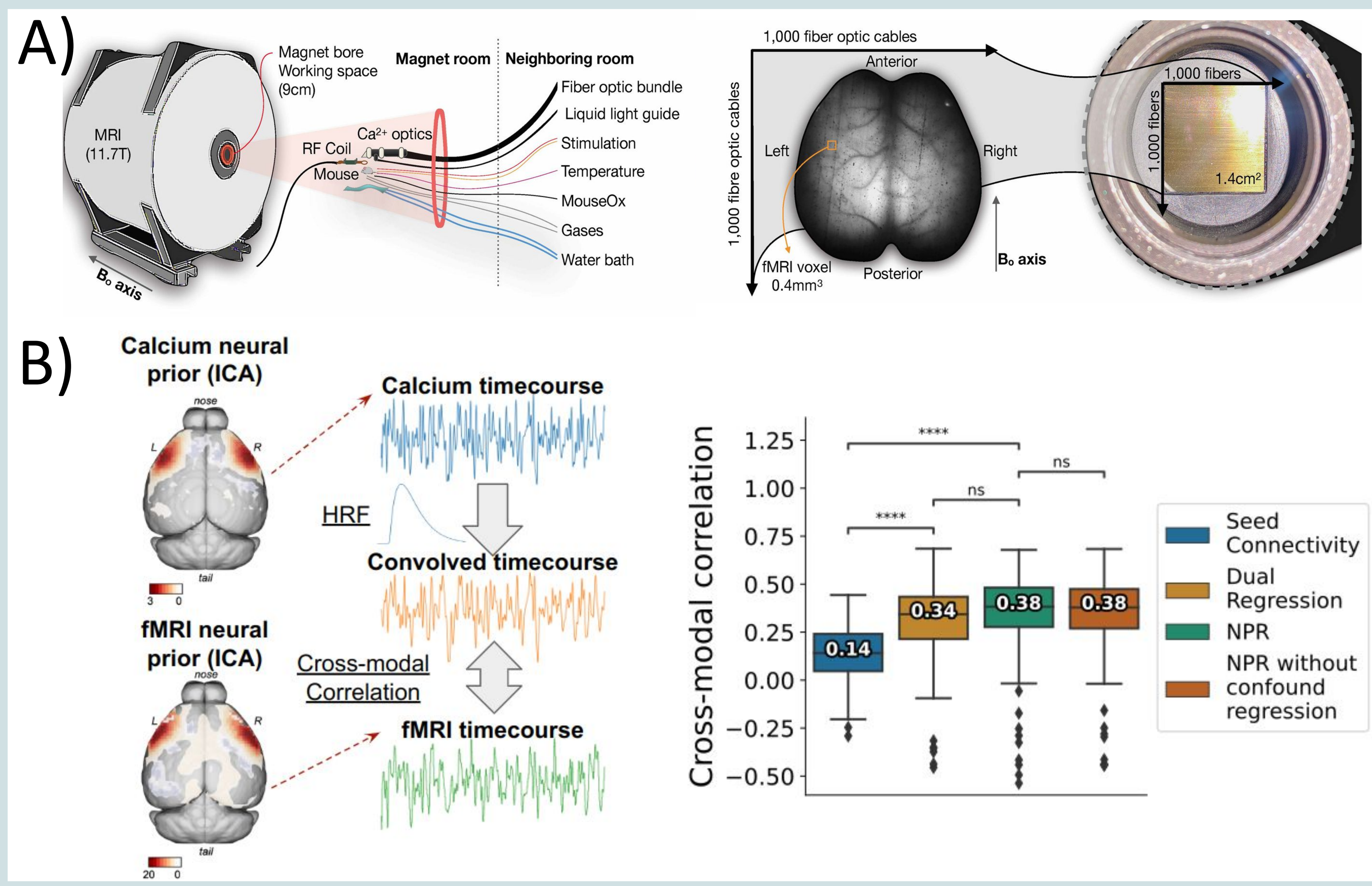


Figure 3: A) Using simultaneous calcium and fMRI imaging (figure adapted from Lake et al. 2020), **B)** a prior of the somatomotor network was identified through group ICA in each modality independently (displayed on 2D cortical surface). A network timecourse is derived in each modality, and the two timecourses are then correlated after hemodynamic response function convolution of the calcium timecourse (gamma variate function: time to peak = 2.6 s, width = 1.2 s). fMRI confound correction consisted of scrubbing + highpass 0.01Hz + motion/WM/CSF regression.

Acknowledgements

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Implications

- We offer a generalizable framework for carrying automated confound correction while preserving neural activity. Can be carried out similarly in human studies.
- **Trade-off:** constrained to the set of priors, discard residuals. But in most studies, residuals are unknown (i.e. without validated neural origin).
- Open source code implemented in RABIES https://github.com/CoBrALab/RABIES